Scientific Abstract

This Phase 2a multicenter, randomized, double-blind, placebo-controlled, dose-escalating safety and efficacy study will evaluate the effects of several dose levels of intramyocardial pVGI.1(VEGF2) plasmid deoxyribonucleic acid (DNA) delivered by percutaneous cardiac catheterization in patients with refractory and stable exertional angina. The pVGI.1(VEGF2) plasmid contains the complementary DNA sequence for the vascular endothelial growth factor 2 protein, a member of a class of natural growth factors that promote angiogenesis. This study will obtain information regarding the safety and effect of this gene for the potential relief of angina.

The primary objectives of this study in adult patients with refractory and stable exertional angina are as follows:

- To assess the safety of single, defined increasing doses of pVGI.1(VEGF2) versus placebo given by intramyocardial injection using percutaneous cardiac catheterization as determined by frequency, severity, and duration of treatment-emergent adverse effects

- To assess the effects of single, defined increasing doses of pVGI.1(VEGF2) versus placebo given by intramyocardial injection using percutaneous cardiac catheterization on change in angina class and exercise tolerance at 12 weeks when compared with pretreatment assessments

Secondary objectives of this study are as follows:

- To assess the effects of single, defined increasing doses of pVGI.1(VEGF2) versus placebo given by intramyocardial injection using percutaneous cardiac catheterization on change in patient functional status as assessed by the Seattle Angina Questionnaire at 12 weeks when compared with pretreatment assessments

- To correlate the changes in patient functional status, exercise tolerance, and angina class with changes in myocardial perfusion as assessed by myocardial scintigraphy

In addition, this study will evaluate the usefulness of NOGA™ mapping as a means to assess myocardial ischemia by comparing the results obtained by this technique with those obtained by myocardial scintigraphy.

The study will consist of a Pretreatment Period (up to 4 weeks), a Treatment Period (1 day), and a Post-treatment Period (12 weeks). This study will include 18 to 27 patients who will be enrolled sequentially into 3 dosing cohorts. Each cohort will consist of a minimum of 6 patients and a maximum of 9 patients. Within each cohort, patients will be randomized to receive either pVGI.1(VEGF2) or placebo in a 2:1 ratio. Within each cohort, treatment will be sequential for each of the first five patients and will only proceed after review of an individual patient's safety data at Week 1 following treatment. Dosing in successive cohorts will occur only after the preceding cohort has been completed and the last patient in the preceding cohort has been evaluated for safety for at least 1 week following treatment.

During the Post-treatment Period, safety will be evaluated based on the adverse experience profile of the patients and on changes in laboratory values, vital signs, and results of physical examination and ophthalmoscopic examination. The effectiveness of treatment will be evaluated by assessing angina class, exercise tolerance, patient functional status, and perfusion defects using myocardial scintigraphy at 12 weeks after treatment as compared with baseline assessment results.

After completing the Post-treatment Period of this study, all patients will enter a 9-month follow-up protocol (Study VEGF2-CAD-CL-003) to collect long-term safety and efficacy data for a total of 12 months after treatment.